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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/500,135	02/08/2000	David A. Estell	A-68893/DJB/DAV	164

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GENENCOR INTERNATIONAL, INC.  
ATTENTION: LEGAL DEPARTMENT  
925 PAGE MILL ROAD  
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EXAMINER

SAUNDERS, DAVID A

ART UNIT	PAPER NUMBER
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1644

DATE MAILED: 05/07/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No. <u>500,135</u>	Applicant(s) <u>ESTELL et al.</u>
Examiner <u>SAUNDERS</u>	Group Art Unit <u>1644</u>

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

## Status

- ☒ Responsive to communication(s) filed on 3/17/03
- ☐ This action is **FINAL**.
- ☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 1 1; 453 O.G. 213.

## Disposition of Claims

- ☒ Claim(s) 2, 5, 7, 14, 29-34, 39, 41 is/are pending in the application.
- ☐ Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- ☒ Claim(s) 2, 5, 7, 14, 29-34, 39, 41 is/are rejected.
- ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- ☐ Claim(s) \_\_\_\_\_ are subject to restriction or election requirement.

## Application Papers

- ☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
- ☐ The proposed drawing correction, filed on \_\_\_\_\_ is ☐ approved ☐ disapproved.
- ☐ The drawing(s) filed on \_\_\_\_\_ is/are objected to by the Examiner.
- ☐ The specification is objected to by the Examiner.
- ☐ The oath or declaration is objected to by the Examiner.

## Priority under 35 U.S.C. § 119 (a)-(d)

- ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- ☐ All ☐ Some\* ☐ None of the CERTIFIED copies of the priority documents have been received.
- ☐ received in Application No. (Series Code/Serial Number) \_\_\_\_\_
- ☐ received in this national stage application from the International Bureau (PCT Rule 1 7.2(a)).

\*Certified copies not received: \_\_\_\_\_

## Attachment(s)

- ☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). \_\_\_\_\_
- ☒ Notice of Reference(s) Cited, PTO-892
- ☐ Notice of Draftsperson's Patent Drawing Review, PTO-948
- ☐ Interview Summary, PTO-413
- ☐ Notice of Informal Patent Application, PTO-152
- ☐ Other \_\_\_\_\_

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The amendment of 3/17/03 has been entered. Claims 2, 5, 7, 14, 29-34, 39 and 41 are pending and under examination.

Applicant's amendment has overcome the previously stated 102 rejection over Carr (WO 98/52976).

Claims 2, 5, 7, 14, 29-34 and 39 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 2 recites new matter.

Applicant has no original disclosure support for reciting "wherein said kinase is not streptokinase", because applicant's disclosure never recited "streptokinase" as a species of kinase. Applicant cannot exclude what was not specifically recited. Ex parte Grasselli 218 USPQ 769.

Upon reconsideration, the following new prior art rejection is stated.

Claim 41 is rejected under 35 U.S.C. 102(a) as being anticipated by Estell (WO 99/53078).

Citation of this reference is proper since the inventive entity differs from that instantly and since the Markush group of claim 41 has no descriptive support in parent application 060,872. See MPEP 201.11.

Estell discloses proteases having a T-cell epitope altered at two or more residues. See page 11, lines 1 and 18; page 14,

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line 3; page 16, line 35. Note that recitations of "one or more amino acids" clearly encompasses and thus anticipates instant recitation of "at least two amino acid residues."

Note, also, that Estell teaches a T-cell epitope can be modified such that "the amino acid sequence is substituted with an analogous sequence from the human subtilisin of the invention to the protein of interest". See page 8, lines 24. Estell then identifies residues 170-173 of the *Bacillus Lentus* subtilisin as corresponding to the allergenic T-cell epitope. See Example 2, at pages 21-22. If these residues of *B. Lentus* (YPAR) are replaced with the aligned residues of human subtilisin (NPAD), one would have at least two substitutions (positions 170 and 173) in accord with instant claim 41. See Fig. 8 of instant application for the alignment of *B. lentus* (savinase) and human (S2HSBT) subtilisin. Claim 41 is this anticipated.

Weisberger et al. (6,495,136) are cited as of interest. They teach proteases/subtilisins having reduced immunogenicity. They teach that subtilisin BPN' may be altered by amino acid modifications at one or more residues within one or more of three epitopic regions. The first epitopic region is constituted by residues 70-84, the second by residues 103-126, and the third by residues 217-254. To one or more of these substituted residues a covalently attached addition moiety (e.g.

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a polymer) is provided. It appears that at least some of the substitutions are effected to provide amino acid residues with a side chain that can couple to the polymer (e.g. col. 11, lines 13-20).

Weisberger et al. Do not teach how the three epitopic regions are identified. It is not clear whether these are B cell or T cell epitopes. The only T cell proliferation assay shown is that conducted with the final, polymer conjugated product, rather than with peptide fragments of the parent or altered peptide. (col. 15, lines 48+). There is thus no direct teaching to alter T cell epitopes per se.

Given the fact that Weisberger et al. do not clearly direct one to make amino acid modifications specifically in T-cell epitopes and the fact that they conjugate polymers at one or more of the substituted amino acid residues, it appears that their taught substitutions per se are not considered sufficient to reduce the immunogenicity of the BPN' subtilisin. Weisberger et al. are thus not cited against any of the instant claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David A. Saunders, Ph.D., whose telephone number is (703) 308-3976. The examiner can normally be reached on Monday-Thursday from 8:00

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a.m. to 5:30 p.m. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan , can be reached on (703) 308-3973. The fax phone number for the organization where this application or proceeding is assigned is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

D. Saunders:jmr

April 9, 2003

*David A. Saunders*

DAVID SAUNDERS  
PRIMARY EXAMINER  
ART UNIT 182/1644